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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

CHOWDHURY, IQBAL HOSSAIN

ART UNIT PAPER NUMBER

1652

DATE MAILED: 02/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/527,090	Applicant(s) YUUKI ET AL.	
	Examiner Iqbal Chowdhury, Ph.D.	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 March 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>3/10/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This application is a 371 of PCT/JP03/11473 filed on 09/09/2003.

Claims 1-24 are pending and are at issue, and will be examined herein.

Claim Objections

Claims 7 and 19 are objected to because of the following informalities: "a" should be inserted before transformant. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-4, 6, 7-16, and 18-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The recitation "derived from Streptomyces" in claims 1, 7, 8, 9, 13, and 19 renders the claim(s) indefinite because it is unclear if the term derived includes only the wild type sequence or includes mutants, variants or fragments thereof, which are unknown, thereby rendering the scope of the claim(s) indefinite. The recitation "derived" can be replaced with "isolated".

Claims 6, 12, 18 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the present instance, claims 6, 12, 18 and 24 recite the "mutant strain thereof" which is unclear as to the scope of mutant strains that are

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encompassed. In another words, how many changes can be made to the microbial strain and still be a “mutant strain thereof”?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a wild type or mutant strains of *Streptomyces* (S.) *mobaraensis* or *S. lividans* comprising wild type transglutaminase or mutant gene obtained by modifying a part of the wild type sequence derived from *S. mobaraensis*, cloning in an expression vector with promoter and terminator for expression of the polypeptide (wild type or mutant) and collecting the produced transglutaminase.

The specification teaches the structure of only two representative species of such DNAs used to produce transformed wild type or mutant strains. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding any transglutaminase to be used to produce transformed wild type and mutant strains. Given this lack of description of representative species encompassed by the genus of DNAs used to produce transformed wild type or mutant strains, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written

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description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a wild type *S. mobaraensis* or *S. lividans* strains comprising wild type transglutaminase gene of SEQ ID NO: 1 or a fragment of SEQ ID NO: 2 encoding a transglutaminase, cloning in an expression vector with promoter and terminator for expression of the polypeptide and collecting the produced transglutaminase, does not reasonably provide enablement for any transformant of *S. mobaraensis* or *S. lividans* strains comprising any wild type transglutaminase or mutant gene obtained by modifying a part of the sequence of SEQ ID NO: 1 or a fragment of SEQ ID NO: 2 derived from *S. mobaraensis*, cloning in an expression vector with promoter and terminator with unknown structure for expression of the polypeptide (wild type or mutant) in the said bacterial strains and collecting the produced transglutaminase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

These claims are so broad as to encompass any transformant of *S. mobaraensis* or *S. lividans* strains comprising any wild type transglutaminase *S. mobaraensis* or any mutant gene obtained by modifying a part of the sequence of SEQ ID NO: 1 or 2 derived from *S. mobaraensis*, cloning in an expression vector with promoter and terminator with unknown structure for expression of the polypeptide (wild type or mutant) in the said bacterial strains and collecting the produced transglutaminase. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to any transformant of *S. mobaraensis* or *S. lividans* strains comprising any wild type transglutaminase or any mutant gene obtained by

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modifying a part of the sequence of SEQ ID NO: 1 or 2 broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the two-nucleotide sequences encoding amino acid sequence of only one protein.

While recombinant and mutagenesis techniques are well known in the art, it is not routine in the art to prepare a bacterial strain comprising either wild type or mutant strains by introducing any wild type or mutant gene as the positions within a protein coding sequence of the genes where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any gene and the result of such modifications is unpredictable in the context of preparing any transformant. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions in the context of preparing any transformant.

The specification does not support the broad scope of the claims which encompass any transformant of *S. mobaraensis* or *S. lividans* strains comprising any wild type transglutaminase or any mutant gene obtained by modifying a part of the sequence of SEQ ID NO: 1 or 2 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting its activity; (B) the general tolerance of the protein to modification and extent

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of such tolerance; (C) a rational and predictable scheme for modifying any protein residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any transformant of *S. mobaraensis* or *S. lividans* strains comprising any wild type transglutaminase or any mutant gene obtained by modifying a part of the sequence of SEQ ID NO: 1 or 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, any transformant either wild type or mutant strains of *S. mobaraensis* or *S. lividans* strains comprising wild type transglutaminase or mutant gene obtained by modifying a part of the sequence of SEQ ID NO: 1 or 2, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for

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patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 13-24 are rejected under 35 U.S.C. 102(e) as being anticipated by Taguchi et al. (WO 01/29187 A1, "Process for producing microorganism-origin transglutaminase", Ajinomoto Co., Inc., see IDS). Taguchi et al. disclose a process for producing microorganism-origin (*Streptomyces mobaraensis*) transglutaminase in transformant and the sequence of a transglutaminase (SEQ ID NO: 3) which is 100% identical to SEQ ID NIO: 1 and the coding sequence of SEQ ID NO: 2 of the instant application. Taguchi et al. also disclose that gene is derived from *S. mobaraensis* with natural promoter and terminator. Taguchi et al. further disclose the cloning the cDNA in expression vector and producing transformant *S. lividans* comprising the expression vector containing the sequence of a transglutaminase gene to produce transglutaminase in high efficiency. Taguchi et al. also mutated the transglutaminase gene and transformed *S. lividans*.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taguchi et al. (WO 01/29187 A1, "Process for producing microorganism-origin transglutaminase", Ajinomoto Co., Inc., see IDS). Taguchi et al. disclose a process for producing microorganism-origin (*S. mobaraensis*) transglutaminase in transformant and the sequence of a transglutaminase (SEQ ID NO: 3) which is 100% identical to SEQ ID NIO: 1 and the coding sequence of SEQ ID NO: 2 of the instant application. Taguchi et al. also disclose that gene is derived from *S. mobaraensis* with natural promoter and terminator. Taguchi et al. further disclose the cloning the cDNA in expression vector and producing transformant *S. lividans* comprising the expression vector containing the sequence of a transglutaminase gene to produce transglutaminase in high efficiency. Taguchi et al. also mutated the transglutaminase gene and transformed *S. lividans*. Taguchi et al. do not disclose transforming *S. mobaraensis* comprising sequence of a transglutaminase gene.

A skill artisan would have motivated to express the gene of transglutaminase with natural promoter and terminator from *S. mobaraensis* to produce a recombinant strain of same host *S. mobaraensis* to produce transglutaminase in increased level. Therefore, it would have been obvious to one of ordinary skill in the art to use the transglutaminase gene with promoter and terminator derived from *S. mobaraensis* of Taguchi et al. to produce a transformant of *S. mobaraensis* (same host) or mutant strain to produce transglutaminase in high efficiency with

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expectation that naturally occurring promoter of transglutaminase gene derived from same *S. mobaraensis* and naturally occurring regulatory proteins presence in the same organism would allow high efficiency of transglutaminase production by binding to the regulatory sequence by enhancing the transcriptional activity as well as preventing degradation over other species as taught by Taguchi et al.

Conclusion

Status of the claims:

Claims 1-24 are pending.

Claims 1-24 are rejected.

No claim is in condition for allowance.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

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